REMARKS

Claims 3-13 are pending in the present application. Claims 3, 4, 5, 6, 11, 12, and 13 have been amended. Thus, upon entry of the amendments presented herein, claims 3-13 will remain pending.

Support for the amendments to the claims may be found in the claims as originally filed and throughout the specification. Specifically, support for the amendment to claim 3 may be found in the specification, at least at page 28, line 7. Support for the amendment to claim 4 can be found in the specification at least at page 17, line 10. No new matter has been added.

The foregoing amendments should in no way be construed as an acquiescence to any of the Examiner's rejections, and have been made solely in the interest of expediting the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed or as previously pending, in this or in one or more separate applications.

Withdrawal of Certain Rejections

Applicants gratefully acknowledge the withdrawal of the following rejections: (a) the previous provisional rejection of claims 3-13 under the judicially created doctrine of obviousness-type double patenting; (b) the previous rejection of claims 11 and 13 under 35 U.S.C. § 112, second paragraph; (c) the previous rejection of claims 3-10,12 and 13 under 35 U.S.C. § 102(e); and (d) the previous rejection of claims 3-13 under 35 U.S.C. § 103(a).

Claim Objections

The Examiner has objected to claims 3, 6, 11, 12 and 13 because, according to the Examiner, these claims do not comply with 37 CFR §§ 1.821-1.825. Accordingly, Applicants have amended claims 3, 6, 11, 12 and 13 such that these claims are now in compliance with 37 §§ CFR 1.821-1.825. Specifically, single letter amino acid abbreviations have been replaced by the corresponding three letter abbreviations. Accordingly, Applicants request that the objection to these claims be reconsidered and withdrawn.

Provisional Rejection of Claim 6 Under the Judicially Created Doctrine of Obviousness-Type Double Patenting

The Examiner has provisionally rejected claim 6 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-21 of copending Application No. 09/643,260. In particular, the Examiner is of the opinion that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the claims 19-21 in U.S. Patent Application 09/643,260 are directed to SEQ ID NO:2, which comprises Leu-Asp-Trp-Ser-Trp-Leu (current application, SEQ ID NO:33, claim 6)."

While in no way admitting that claim 6 of the present application is obvious over claims 19-21 or co-pending Application No. 09/643,260, upon allowance of the '260 application Applicants will consider submitting a terminal disclaimer in that application in compliance with 37 C.F.R. 1.321(b) and (c), if appropriate, which will obviate this rejection.

Rejection of Claims 3-5 and 7-11 Under 35 U.S.C. 112, Second Paragraph

The Examiner has rejected claims 3-5 and 7-11 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically, the Examiner has taken the position that the variable X_a in claim 3 is indefinite and, citing to M.P.E.P. § 2111, argues that "[r]eading a claim in light of the specification, to thereby interpret limitations explicitly recited in the claim, is quite a different thing from reading limitations of the specification into a claim, to thereby narrow the scope of the claim by implicitly adding disclosed limitations which have no express basis in the claim."

Applicants respectfully traverse this rejection for the following reasons. Contrary to the Examiner's allegations, Applicants are not improperly reading limitations of the specification into the claims. Rather, Applicants are reading the claims in light of the specification. M.P.E.P. § 2111 expressly provides that "[d]uring patent examination, the pending claims must be 'given *>their< broadest reasonable interpretation ***consistent with the specification***'" (***Emphasis added***. In *re Hyatt*, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000)) and M.P.E.P. § 2111.01 provides that "the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification." In the present case, the variable X_a, a membrane transduction domain, is explicitly defined in the specification at page 18, lines 24-34 (see Applicants' Amendment and Respose dated July 15, 2004) and, thus, the skilled artisan reading the claims in light of the specification would find this term to be clear and

definite. The Examiner has not provided any reason why one of ordinary skill in the art would not understand the term "X_a" after reading the ***explicit*** definition provided by Applicants in the specification. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection as it applies to claim 3 and claims depending therefrom.

With respect, in particular, to claim 4, the Examiner argues that the variable X_a of claim 4 can not be both 6 to 15 amino acids in length and the amino acid sequence TA (Thr-Ala). In the interest of expediting prosecution of the present application, Applicants have amended claim 4 to substitute X_a with the amino acid sequence TA (Thr-Ala), reflecting the intended embodiment of claim 4 as originally presented. Accordingly, Applicants request that the Examiner reconsider and withdraw this rejection.

The Examiner has also rejected claim 5, stating that it is not clear where the additional amino acids of X_7 are part of the claimed anti-inflammatory compound. Applicants respectfully traverse this rejection because it is clear based on the claim language that the progression of variable domains in the anti-inflammatory compound is in ascending numerical order. However, in the interest of expediting prosecution of the present application, Applicants have amended claim 5 to indicate that X_7 is located immediately C-terminal to X_6. Applicants, therefore, request that the Examiner reconsider and withdraw this rejection.

Rejection of Claims 3-10 Under 35 USC § 102(b)

The Examiner has rejected claims 3-10 under 35 U.S.C. § 102(b) as being anticipated by Rothe *et al.* (WO 99/01541). In particular, the Examiner is of the opinion that

> Rothe et al. teach SEQ ID NO: 2 comprising: TALDWSWLQTE at amino acid residues 735-745. Therefore, Rothe et al. teach compounds comprising TALDWSWLQTE, LDWSWLQTE, TALDWSWL, ALDWSWLQTE, LDWSWLQTE, LDWSWL, TALDWSWLQT, TALDWSWLQ, ALDWSWLQT, LDWSWLQ, and LDWSWLQT. In SEQ ID NO: 4, LDWSWL is taught at ammo acid residues 738-743, and peptides comprising the sequence are taught on page 4, line 9 as residues 737-745. Therefore, Rothe et al teach compounds comprising LDWSWL.

The Examiner also states that "[t]he amino acid sequence described [by] Rothe et al. inherently possesses the functional qualities of the anticipated fusion protein" and that "[i]t is recognized by a person of ordinary skill in the art that a disclosed protein structure will always produce a function based on structure."

Applicants respectfully traverse this rejection for the reasons of record. However, in the interest of expediting prosecution of the instant application, Applicants have amended the claims such that they are now directed to anti-inflammatory compounds which are less than 100 amino acids in length.

For a prior art reference to anticipate a claimed invention under 35 U.S.C. § 102, the reference must teach ***each and every element*** of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d. 744, 3 USPQ2d 1766 (Fed. Cir. 1987). Rothe *et al.* disclose IKK-α polypeptides which are 756 amino acids (SEQ ID NO:2) and 745 amino acids (SEQ ID NO:4) in length. Rothe *et al.* do not teach or suggest anti-inflammatory compounds comprising a NEMO binding domain fused to a membrane translocation domain, wherein the compounds are less than 100 amino acids in length. Accordingly, Rothe *et al.* do not anticipate the pending claims and Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Rejection of Claims 3-13 Under 35 U.S.C. § 103(a)

The Examiner has also rejected claims 3-13 under 35 U.S.C. § 103(a) as being unpatentable over Rothe *et al.* (WO 99/01541). In particular, the Examiner is of the opinion that "in view of Applicants admissions, all claimed peptides are rendered obvious over the teachings of Rothe *et al.*"

Applicants respectfully traverse this rejection for the reasons of record and the following reasons. To begin with, Applicants never admitted that Rothe *et al.* teaches the sequences TALDWSWLQTE and LDWSWLSEQ. Applicants merely indicated that Rothe *et al.* disclose the sequences of IKK-α polypeptides which comprise the foregoing sequences. Specifically, Rothe *et al.* disclose IKK-α polypeptides which are 756 amino acids (SEQ ID NO:2) and 745 amino acids (SEQ ID NO:4) in length. There is no teaching or suggestion in Rothe *et al.* regarding anti-inflammatory compounds comprising a NEMO binding domain fused to a membrane translocation domain, wherein the compounds are less than 100 amino acids in length. Accordingly, the teachings of Rothe *et al.* fail to render the claimed invention obvious and Applicants request that the Examiner reconsider and withdraw this rejection.

Rejection of Claims 3-13 Under 35 U.S.C. § 103(a)

The Examiner has also rejected claims 3-13 under 35 U.S.C. § 103(a) as being unpatentable over Rothe *et al.* (WO 99/01541), in view of Schwarze *et al.* (1999) *Science* 285: 1569-1572. Specifically, the Examiner is of the opinion that

> Schwarze et al. discloses efficient delivery of therapeutic compounds into cells using the amino terminal 11 amino acid protein transduction domain from human immunodeficiency virus TAT protein, which is the first 11 amino acids of SEQ ID NO: 133 disclosed in claim 12 (see entire document, particularly 2nd paragraph of Introduction, and the sequence disclosed in reference 7). One would have been motivated to fuse the amino acid sequence disclosed by Rothe et al. with the transduction domain disclosed by Schwarze et al. to increase transduction of the therapeutic peptide into a cell. It would have been obvious to a person having ordinary skill in the art to fuse the amino acid sequence disclosed by Rothe et al. with the protein transduction domain disclosed by Schwarze et al. to deliver the therapeutic peptide compound into cells (current application, claims 3-13).

Applicants respectfully traverse this rejection on the grounds that the Examiner has failed to establish a *prima facie* case of obviousness, since the combination of Rothe *et al.* and Schwarze *et al.* fails to teach or suggest the claimed invention and further fail to provide the necessary motivation or reasonable expectation of success for the ordinarily skilled artisan to have tried making or using the presently claimed anti-inflammatory compounds.

To establish a *prima facie* case of obviousness, it is necessary for the Examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied references, or in the form of generally available knowledge, that one having ordinary skill in the art would have been motivated to make the claimed invention and would have had a reasonable expectation of success in making the claimed invention. Under section 103, "[b]oth the suggestion and the expectation of success must be founded in the prior art, not in applicant's disclosure." (*Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* 927 F.2d 1200, 1207, 18 USPQ2d 1016 (Fed. Cir. 1991), quoting *In re Dow Chemical Co.,* 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed Cir. 1988)). Moreover, when a combination of references are used to establish a *prima facie* case of obviousness, the Examiner must present evidence that one having ordinary skill in the art would have been motivated to combine the teachings in the applied references in the proposed manner to arrive at the claimed invention. See, *e.g.*, *Carella v. Starlight Archery*,

804 F.2d 135, 231 USPQ 644 (Fed. Cir. 1986); and *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc.*, 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985).

The claimed invention is directed to anti-inflammatory compounds comprising a NEMO binding domain fused to a membrane translocation domain, wherein the compounds are less than 100 amino acids in length. This invention is based, at least in part, on the discovery that by blocking NEMO's interaction with the NEMO binding domain (NBD) of IKK-α or IKK-β, cytokine-mediated NF-κB activation can be inhibited, thereby blocking NF-κB-mediated inflammatory responses.

As discussed above, the primary reference of Rothe *et al.* merely discloses the amino acid sequences of human IKK-α polypeptides which are 756 amino acids (SEQ ID NO:2) and 745 amino acids (SEQ ID NO:4) in length. Rothe *et al.* fail to teach or suggest that there is a NEMO binding domain within IKK-α. Rothe *et al.* also fail to teach or suggest that the disclosed IKK-α polypeptide possesses the anti-inflammatory properties of the claimed peptide compounds. In fact, one of ordinary skill in the art would not expect the full-length IKK-α polypeptides disclosed in Rothe *et al.* to exert the anti-inflammatory properties of the short (<100 amino acids), membrane-translocating, NBD-containing polypeptides of the instant invention because, *inter alia*, administered full-length IKK-α proteins would not be expected to achieve cytosolic localization absent a membrane-translocating domain. Accordingly, Rothe *et al.* fail to teach or suggest the claimed invention.

Moreover, the secondary reference of Schwarze *et al.* fails to make up for the aforementioned deficiencies in the primary reference of Rothe *et al.* Specifically, Schwarze *et al.* teach the use of an HIV TAT polypeptide in the context of a fusion protein (*e.g.*, TAT-FITC or TAT-β-Gal), allowing for distribution of the fusion protein throughout the cells of an animal, including partitioning of the fusion protein across the blood-brain-barrier (BBB). However, Schwarze *et al.* do not teach or suggest synthesis of fusion proteins comprising the NBD sequences of the instant invention. Additionally, absent the teachings of the instant specification, one of ordinary skill in the art would have had no motivation to combine the TAT polypeptides featured in Schwarze *et al.* with the human IKK-α polypeptides disclosed in Rothe *et al.*, to generate the therapeutic NBD fusion proteins of the instant invention, as there is no teaching or suggestion in either Rothe *et al.* or Schwarze *et al.* motivating the skilled artisan to do so.

For the foregoing reasons, the anti-inflammatory compounds of claims 3-13 are non-obvious, and thus patentable, over Rothe *et al.* in view of Schwarze *et al.* Accordingly, Applicants respectfully request that the rejection of claims 3-13 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

SUMMARY

In view of the above, each of the presently pending claims in this application is believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Applicants also file an appropriate extension of time herewith and believe that no further fee is due with this statement. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. YAI-002 from which the undersigned is authorized to draw.

Dated: March 7, 2005

Respectfully submitted,

By _____

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